REMARKS

Reconsideration of the present application is respectfully requested in view of the above Amendments and following remarks. Claims 54-59 were currently pending. As an initial matter, Applicants note that the Office Action Summary lists claims 57-59 as pending under Disposition of Claims. Because claims 54-59 were discussed throughout the Office Action and Applicants' records also indicate claims 54-59 were pending, Applicants assume that this listing in the Disposition of Claims is a typographical error. Applicants hereby cancel claim 59 without acquiescence to any rejection and without prejudice to pursuing the cancelled subject matter in a related divisional, continuation, or continuation-in-part application. Applicants have added new claim 60 to point out with greater particularity and distinctly claim certain embodiments of Applicants' invention. No new matter has been added by these amendments. Support for the new claim may be found throughout the application, for example, at page 13, lines 21-34. Upon entry of the amendments submitted herewith, claims 54-58 and 60 will be pending and under examination.

DOUBLE PATENTING

A. The Examiner asserts that claims 54-59 of the instant application conflict with claims 18-20, 22 and 35-38 of U.S. Application No. 10/476,614 ('614). The Examiner asserts that absent good and sufficient reason, Applicants are required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications.

B. The Examiner provisionally rejected claims 54 and 57 under 35 U.S.C. § 101 for alleged statutory double patenting over claims 18 and 37 of co-pending U.S. Application No. 10/476,614 ('614). The Examiner asserts that despite the minor differences in wording, the claims in each of the above-identified applications recite the same structures and, therefore, claim the same invention.

Applicants respectfully traverse these rejections and submit that the presently claimed subject matter is patentably distinct from the claimed subject matter in the '614

application. As an initial matter, Applicants note that claim 59 has been canceled without acquiescence or prejudice, rendering moot the rejection of this claim.

Applicants submit that claims 54-58 of the instant application do not conflict with any claims pending in the '614 application. The claims in each application recite *different* structures, and thus encompass *different* (*i.e.,* non-overlapping) inventive subject matter. For example, claim 54 of the instant application relates to a group A *Streptococcus* (*i.e., S. pyogenes*) polypeptide, and variants thereof, (referred to in the application as BVH-P7), comprising an amino sequence at least 95% identical to the amino acid sequence SEQ ID NO:2 (see Sequence Listing). By contrast, presently pending claim 18 of the '614 application relates to a group B *Streptococcus* (*i.e., S. agalactiae*) polypeptide, and variants thereof, (referred to in the '614 application as BVH-A4), that comprises an amino acid sequence at least 95% identical to an exemplary amino acid sequence of the BVH-A4 polypeptide, also having the sequence identifier SEQ ID NO:2. As stated in the Office Action dated May 27, 2004, an amino acid sequence alignment shows that the group A streptococcal BVH-P7 polypeptide of the instant application shares less than 75% amino acid sequence identity with the group B streptococcal BVH-A4 polypeptide of the '614 application. Given this difference in sequence identity, the claims in each application are directed to structurally distinct polypeptide sequences and, therefore, do not overlap or conflict in scope. Accordingly, the subject matter of claims 54-58 of the present application and claims 18-20, 22 and 35-38 of the '614 application do not conflict, and Applicants respectfully request that this rejection be withdrawn.

Applicants also submit that claims 54 and 57 of the instant application encompass patentably distinct subject matter from that recited in claims 18 and 37 of the '614 application; therefore, the present claims comply with the statutory requirements under 35 U.S.C. § 101. As discussed above, the claimed group A *Streptococcus* BVH-P7 polypeptide as recited in claims 54 and 57 in the present application does not have the same structure as the group B *Streptococcus* polypeptide BVH-A4 as claimed in claims 18 and 37 of the co-pending '614 application. Accordingly, Applicants respectfully request withdrawal of the provisional statutory double patenting rejection of claims 54 and 57.

Nonetheless, if the Examiner maintains this statutory double patenting rejection, Applicants submit that when the *provisional* statutory double patenting rejection is the only rejection remaining in this application, the Examiner should withdraw the rejection as required under M.P.E.P § 804(I)(B)(2).

REJECTIONS UNDER 35 U.S.C. § 102

The Examiner rejected claim 54 under 35 U.S.C. § 102(a), asserting that the claimed subject matter lacks novelty over Ferretti et al. (*Proc. Natl. Acad.* Sci. USA 98(8):4658-4663, April 2001). The Examiner asserts that claim 54 is not entitled to the February 21, 2001 priority date, but is instead entitled only to the February 21, 2002 filing date, because the priority application (U.S. Provisional Application No. 60/269,840) allegedly fails to describe the claimed polypeptide "variants" in a manner that satisfies the written description requirement under 35 U.S.C. § 112, first paragraph.

Applicants respectfully traverse this rejection and submit that claim 54 is novel over Ferretti et al. because the cited document is not valid prior art. Claim 54 is directed to a polypeptide comprising an amino acid sequence at least 95% identical to SEQ ID NO:2, which polypeptide is capable of eliciting an immune response to *Streptococcus pyogenes* and eliciting an antibody that specifically binds to a BVH-P7 polypeptide that consists of the amino acid sequence set forth in SEQ ID NO:2. Applicants submit that the polypeptide variants are sufficiently described in U.S. Provisional Application No. 60/269,840 ('840), filed February 21, 2001, ***before*** the publication date of Ferretti et al., to convey to a person skilled in the art that Applicants possessed the presently claimed embodiments.

Applicants respectfully submit that the Examiner has not established a *prima facie* case for lack of written description. The Office Action states that, "[i]t has been determined that claim 54 is only entitled to the instant filing date because the provisional document fails to comply with the written description requirement for the variants" (Action, page 5, lines 5-7). The Examiner has the initial burden of presenting *evidence or reasons* why a person skilled in the art would not recognize that the written description of the invention provides support for the claims; however, neither evidence nor reasons have been provided for this rejection. *See*

M.P.E.P. § 2163. A similar statement was made in the Office Action dated March 8, 2007 that such reasons were "made of record" (*see* page 8 of the March 8, 2007 Action), yet this Action was the first paper issued by the U.S. Patent and Trademark Office asserting that any claims were anticipated by Ferretti et al. because the provisional application lacked written description.

After reviewing the record, Applicants can find no *evidence or reasons* that the Examiner has presented to support the assertion that the '840 provisional application fails to support polypeptides comprising at least 95% amino acid sequence identity to the BVH-P7 polypeptide of SEQ ID NO:2. Indeed, in the Office Action dated October 14, 2005, the Examiner agrees that claims directed to isolated *S. pyogenes* polypeptides comprising at least 95% identity to the amino acid sequence set forth in SEQ ID NO:2 meet the written description provision of 35 U.S.C. § 112, first paragraph (*see* Office Action dated October 14, 2005, page 8, first full paragraph). In this Action and in accordance with these statements, the Examiner has withdrawn the rejections under 35 U.S.C. § 112, first paragraph. Applicants therefore submit that claim 54 is entitled to the February 21, 2001 priority date of the '840 application and that Ferretti et al. fail to teach or suggest the subject matter of claim 54.

Nonetheless, Applicants submit that the '840 priority application satisfies the written description requirement with respect to polypeptides that comprise an amino acid sequence at least 95% identical to SEQ ID NO:2 and that are capable of eliciting an immune response to *S, pyogenes* and eliciting an antibody that specifically binds to a BVH-P7 polypeptide consisting of the sequence of SEQ ID NO:2. Description that is needed in a specification to support generic claims related to biological subject matter depends on a variety of factors, including "existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter." *Capon v. Eshhar,* 418 F.3d 1349, 1359 (Fed. Cir. 2005). Thus, the fundamental factual inquiry under the written description requirement focuses on the understanding of *a person skilled in the art.* M.P.E.P. § 2163.02. The written description requirement can be met by disclosure of sufficiently detailed, relevant identifying characteristics such as structure, physical properties, or functional characteristics when correlated with a known or disclosed structure, or some combination of such

characteristics. *Enzo Biochem v. Gen-Probe*, 323 F.3d 956, 964 (Fed. Cir. 2002). Here, given the high-level of understanding in the molecular biology and microbiology arts, the '840 priority application describes sufficiently detailed structural features of the claimed, highly related polypeptides (*i.e.,* 95% identity to the recited amino acid sequence of SEQ ID NO:2) and correlates those structural features with the recited functional characteristics (*i.e.,* the capability to raise antibodies to the polypeptide of SEQ ID NO:2 and to induce an immune response to *S. pyogenes*), such that a person skilled in the art would recognize that Applicants possessed the presently claimed subject matter at the time of filing.

The '840 priority application describes an exemplary amino acid sequence (*e.g.,* SEQ ID NO:2) of a *S. pyogenes* cell surface polypeptide referred to in the application as BVH-P7 (*see, e.g.,* page 3, lines 13-15; Figure 2) and that a variant of this polypeptide may have an amino acid sequence at least 95% identical to SEQ ID NO:2, as recited in claim 54 (*see, e.g.,* '840 application, page 4, lines 3-5). The '840 application also states that the BVH-P7 polypeptide and variants thereof may include one or more additions, deletions, or substitutions, such as those substitutions having a minimal influence on the secondary structure and hydropathic nature of the polypeptide (*see, e.g.,* '840 application, page 5, lines 13-34). From this description, and given the routine nature of substituting one or more amino acid residues in a given polypeptide, a person skilled in the molecular biological art would recognize that Applicants not only contemplated and described the sequence set forth in SEQ ID NO:2, but, contrary to the Examiner's assertion (*see* the Action, page 5), contemplated and described a genus of structurally related "variant" polypeptides having 95% sequence identity to SEQ ID NO:2. Indeed, only when a person skilled in the art is given Applicant's disclosure of the nucleotide sequence and the encoded amino acid sequence of this *S. pyogenes* polypeptide, is the skilled person able to recognize such variants.

Furthermore, a person skilled in the art would recognize that the '840 application describes multiple, representative polypeptide variants of SEQ ID NO:2 as shown by the PCR-based identification of BVH-P7 genes and immunological characterization of the encoded polypeptides from four serologically distinct *S. pyogenes* strains (*see, e.g.,* Table 2, starting on page 20, line 26). Moreover, the '840 application describes the correlation between the recited

structural features of the polypeptide variants and the recited functional features. For example, the '840 application discloses that the claimed polypeptides (*e.g.,* polypeptides having 95% identity to SEQ ID NO:2) are able to raise antibodies having binding specificity to a polypeptide consisting of SEQ ID NO:2 (*see, e.g.,* page 4 line 33, to page 5, line 2). In addition, the '840 application describes, in working examples, that BVH-P7 polypeptides are capable of raising antibodies having binding specificity to BVH-P7 expressed on the surface of intact cells of numerous strains of *S. pyogenes* (*see, e.g.,* page 26, lines 9-34 of the '840 application).

Indeed, as here, even when a bacterial antigen such as BVH-P7 is conserved among various strains of a bacterial species, a person skilled in the microbiology or molecular biology arts would not reasonably expect, given the rapid division time of a bacterium and the genetic adaptability of an infectious disease organism in a host, that the polynucleotide sequence and the encoded BVH-P7 polypeptide sequence in each *S. pyogenes* organism would be identical. The skilled person, therefore, would reasonably expect that the polynucleotide and the encoded polypeptide from each strain of *S. pyogenes*, such as those identified in Table 2, would likely have variant nucleotide and amino acid sequences when compared with the exemplary sequences disclosed in SEQ ID NO:1 and SEQ ID NO:2, respectively.

Given also that the '840 application describes in working examples, the ability of the polypeptide of SEQ ID NO:2 to generate antibodies that bind to the BVH-P7 variant proteins encoded by the BVH-P5 genes (*see, e.g.,* page 26, lines 9-34), a person skilled in the art would further recognize that the '840 application describes that the polypeptide variants have structurally related epitopes. The skilled person, therefore, would understand that polypeptides comprising these representative variant sequences are similarly capable of eliciting an antibody that specifically binds to a BVH-P7 polypeptide of SEQ ID NO:2, as recited in claim 54. Moreover, restricting patentable subject matter to the precise, exemplary amino acid sequence of the disclosed *S. pyogenes* polypeptide is unduly limiting and fails to recognize the contribution of the Applicants to discovering and developing immunogenic compositions and vaccines for treating and preventing *S. pyogenes* infections. Given this direct correlation between structure and function, and the corresponding working examples, a person skilled in the art would

recognize that Applicants possessed the BVH-P7 polypeptides of claim 54, including variants having 95% identity thereof, at the time of filing the instant application.

Accordingly, Applicants submit that the '840 provisional application describes the subject matter of claim 54 in sufficient detail to convey to a person skilled in the art that Applicants possessed the claimed subject matter at the time of filing as required under 35 U.S.C. § 112, first paragraph. Therefore, claim 54 is entitled to the '840 priority filing date of February 21, 2001, and accordingly, Ferretti et al. published ***after*** the February 21, 2001 priority date of the instant application is not valid prior art.

Given that Ferretti et al. do not represent valid prior art and that prior to the publication of Ferretti et al., Applicants had described a polypeptide comprising the amino acid sequence of SEQ ID NO:2 and variants thereof, Ferretti et al. fail to destroy the novelty of claim 54. Applicants therefore respectfully request withdrawal of this rejection.

REJECTIONS UNDER 35 U.S.C. § 103

A. The Examiner rejected claim 58 under 35 U.S.C. § 103(a), asserting that the claimed subject matter is obvious over Ferretti et al. in view of Campbell et al. (*Monoclonal Antibody Technology*, Elsevier Science Publishers, 1984, Chapter 1, section 1.3.4, page 29) and Harlow et al. (Cold Spring Harbor Press, 1988, pages 72-73 and 76-77). The Examiner asserts that Ferretti et al. teach a polypeptide that is 100% identical to the polypeptide of SEQ ID NO:2, but agrees that Ferretti et al. do not teach combining the polypeptide with a pharmaceutical carrier, diluent, or adjuvant. The Examiner further asserts that Campbell et al. teach that cloning a gene and making monoclonal antibodies to the encoded polypeptide is "customary." The Examiner further asserts that combining the polypeptide as described in Ferretti et al. with an adjuvant as described by Harlow et al. to make an immunogenic composition would have been obvious to a person having ordinary skill in the art at the time the present application was filed.

Applicants traverse this rejection and submit that the Examiner has not established a *prima facie* case of obviousness. *See In re Mayne*, 104 F.3d 1339 (Fed. Cir. 1997) (The USPTO has the burden of showing a *prima facie* case of obviousness). As discussed in detail above with respect to the rejection of claim 54 under 35 U.S.C. § 102, Ferretti et al. was

published after the February 21, 2001 priority date of the instant application, and each of the present claims is entitled to the February 21, 2001 priority date. Because the priority document (U.S. Provisional Application No. 60/269,840) discloses the polypeptide (referred to therein as BVH-P7) as recited in present claims 54-57 and discloses pharmaceutical compositions comprising these polypeptides as recited in present claim 58, and because Ferretti et al. was not publicly available until ***after*** February 21, 2001, the cited document does not qualify as prior art under 35 U.S.C. §§ 102 or 103.

Even assuming, *arguendo*, that Ferretti et al. qualify as prior art under § 103, Ferretti et al., alone or in combination with either or both of Campbell et al. and Harlow et al., fail to teach or suggest a pharmaceutical composition comprising a polypeptide of SEQ ID NO:2, or variant thereof, that is capable of eliciting an antibody that specifically binds to a BVH-P7 polypeptide and that elicits an immune response to *S. pyogenes*. The Examiner must, at a minimum, demonstrate that either a single reference or a combination of the cited references teaches or suggests all the features of the claim. If the combination of references teaches each claim feature, the Examiner must provide an explicit, apparent reason why a person having ordinary skill in the art would combine these features in the fashion claimed by the Applicants with a reasonable expectation of successfully obtaining the claimed subject matter. *See KSR v. Teleflex, Inc.,* 237 S. Ct. 1727, 1741 (2007) ("[A] patent composed of several elements is not proved obvious merely by demonstrating that each element was, independently, known in the prior art.").

Applicants submit that Ferretti et al., alone or in combination with Campbell et al. and Harlow et al., fail to teach or suggest a pharmaceutical composition that comprises a pharmaceutically acceptable carrier, diluent, or adjuvant and a BVH-P7 polypeptide comprising the amino acid sequence of SEQ ID NO:2, or a variant thereof at least 95% identical to SEQ ID NO:2; a BVH-P7 polypeptide from which the N-terminal methionine residue has been deleted, or a BVH-P7 polypeptide that lacks the signal peptide consisting of the amino acid sequence at positions 1-21 of SEQ ID NO:2 and that have the functional features as recited. Ferretti et al. describe the nucleotide sequence of the genome of a *S. pyogenes* strain and describe more than 1700 open reading frames that putatively encode polypeptides. However, the cited document

fails to teach or suggest which, if any, of the putatively encoded 1700 polypeptides may be useful in a pharmaceutical composition as a vaccine for inducing an immune response to *S. pyogenes*. Thus, a person having ordinary skill in the art would have no reasonable expectation of successfully achieving Applicants' claimed compositions on the basis of the teachings in Ferretti et al. with or without the textbook knowledge set forth in Campbell et al. and Harlow et al., which merely disclose that antibodies (including monoclonal antibodies) may be prepared that specifically bind to a polypeptide of interest.

Contrary to the assertion by the Examiner, a *prima facie* case of obviousness cannot be established by asserting that a person having ordinary skill in the art *could* make a composition, particularly one with no known utility (see Action, page 7 ("…it is now customary to both clone the gene and make monoclonal antibodies to the polypeptide (*sometimes without a clear objective for their application.*") (emphasis added)). With nothing more than the assertion that a person having ordinary skill in the art has the capability to make and *could* make the claimed pharmaceutical composition is insufficient to establish obviousness (*see* M.P.E.P. § 2143.01(IV) ("that the claimed invention is within the capabilities of one of ordinary skill in the art is not sufficient by itself to establish *prima facie* obviousness.")).

Applicants submit that Ferretti et al. is not prior art under 35 U.S.C. § 103(a) and even if Ferretti et al. were proper prior art, claim 58 satisfies the requirements of non-obviousness under 35 U.S.C. § 103(a). Applicants therefore respectfully request withdrawal of this rejection.

B. The Examiner rejected claim 59 under 35 U.S.C. § 103(a), alleging that the claimed subject matter is obvious over LePage et al. (U.S. Application Publication No. 2003/0170782) in view of Harlow et al.

While Applicants strongly disagree with the assertion by the Examiner, the rejection is moot in view of the amendments submitted herewith, which include cancellation of claim 59 without acquiescence to the rejection and without prejudice to pursuing the encompassed subject matter in a related application.

Applicants respectfully submit that claims 54-58 and 60 in the application meet the patentability requirements and are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited. In the event that the Examiner believes a teleconference will facilitate prosecution of this application, the Examiner is invited to telephone the undersigned representative at 206-622-4900.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,

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